(19) World Intellectual Property **Organization**

International Bureau



(43) International Publication Date 17 February 2005 (17.02.2005)

PCT

(10) International Publication Number WO 2005/014822 A2

(51) International Patent Classification7:

C12N 15/62

(21) International Application Number:

PCT/EP2004/051715

(22) International Filing Date: 4 August 2004 (04.08.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/492,397

4 August 2003 (04.08.2003) US

(71) Applicant (for all designated States except US): Applied Research Systems ARS Holding N.V. [NL/NL]; Pietermaai 15, Curacao (AN).

(72) Inventor; and

(75) Inventor/Applicant (for US only): YANG, Meija [US/US]; 6 Catbird Lane, East Lyme, Connecticut 06333 (US).

(74) Agent: SERONO INTERNATIONAL S.A. INTEL-LECTUAL PROPERTY; 12, Chemin des Aulx, CH-1228 Plan-les-Ouates (CH).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- without international search report and to be republished upon receipt of that report
- with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



(57) Abstract: The present invention provides novel therapeutic molecules called Culling Fusion Proteins (CFPs) that allow the continuous removal of therapeutic targets from extracellular space by exploiting the endosome/lysosome intracellular degradation pathway, and the exocytotic pathway in a combined manner. The products of the invention, by appropriately utilizing the cellular endocytosis and exocytosis mechanism, can be recycled multiple times by cells to eliminate undesired molecules, therefore such therapeutic molecules can be administered at low concentration.

